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| PRE-APPEAL BRIEF REQUEST FOR REVIEW | | Docket Number: 08191-0012002 |
| | Application Number 10/758,970 | Filed January 16, 2004 |
| | First Named Inventor Michael Tyo et al. | |
| | Art Unit 1633 | Examiner Ileana Popa |
| | | |
| <p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a Notice of Appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <div style="display: flex; justify-content: space-between; align-items: flex-start;"> <div style="width: 45%;"> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record <u>47,443</u> (Reg. No.)</p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____</p> </div> <div style="width: 45%; text-align: center;"> <p>_____ /Jack Brennan/ Signature</p> <p>_____ Jack Brennan Typed or printed name</p> <p>_____ (212) 765-5070 Telephone number</p> <p>_____ June 18, 2009 Date</p> </div> </div> <p style="font-size: small; margin-top: 20px;">NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below'.</p> | | |
| <input type="checkbox"/> Total of 30 forms are submitted. | | |

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant : | Michael Tyo et al. | Art Unit : | 1633 |
| Serial No. : | 10/758,970 | Examiner : | Ileana Popa |
| Filed : | January 16, 2004 | Conf. No. : | 6224 |
| Title : | CONTINUOUS-FLOW METHOD FOR PREPARING MICROPARTICLES | | |

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants submit this request under the Pre-Appeal Conference Pilot Program described in the U.S. Patent and Trademark OG Notice, "New Pre-Appeal Brief Conference Pilot Program," dated July 12, 2005, and extended until further notice as of January 10, 2006. This request is being filed with a Notice of Appeal.

Status of Claims and Summary of Rejections

Claims 1-55 are pending in the application. In the final Office Action dated December 26, 2008, claims 1-55 were rejected as obvious.

Rejections Under 35 U.S.C. §103(a)

At pages 2-9 of the final Office Action, claims 1-4, 12-17, 19-25, 32-46, 48-50, 54, and 55 were rejected as unpatentable over Shah, U.S. Patent No. 6,020,004, in view of Chen et al., U.S. Patent No. 6,537, 813 ("Chen") and Tice et al., U.S. Patent No. 4,389,330 ("Tice").

Independent claim 1 is directed to a process for preparing nucleic acid-containing microparticles. The method requires "continuous" action at the following steps (maintaining the lettering for the steps used in the claim): (b) continuously supplying a first emulsion to a mixing chamber; (c) continuously supplying a second aqueous solution to the mixing chamber; (d) continuously emulsifying the first emulsion and the second aqueous solution in the mixing chamber to form a second emulsion; and (e) continuously transferring the second emulsion from the mixing chamber to a solvent removal device. An aqueous suspension of nucleic acid-

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containing microparticles is ultimately formed in the solvent removal device in step (f) via diffusion of the organic solvent into an aqueous phase of the second emulsion.

Shah describes “an improved method for preparing polymeric microparticles containing an active ingredient through unique utilization of direct lyophilization of emulsion or suspension” (Shah at column 2, lines 56-59). The “direct lyophilization” methodology of Shah is used to remove aqueous and organic solvents and produce the microparticles (Shah at column 5, lines 63-65). According to Shah “[i]t is utilization of this single step, i.e., direct lyophilization of the final emulsion or suspension, which refines and simplifies the present process over previously described processes, which require multiple steps and are often cumbersome” (Shah at column 6, line 66, to column 7, line 3).

Chen was cited as disclosing a concurrent flow mixing method and apparatus for the preparation of nucleic acid-containing microparticles.

Tice describes a multi-step solvent evaporation process for the preparation of microcapsules.

The Office Action acknowledged (at page 4) that “[n]either Shah, nor Chen et al. teach removing the organic solvent from the second emulsion to form an aqueous suspension of microparticles (step ‘f’ of claim 1).” However, the Office Action asserted (at page 5) that

it would have been obvious to one of skill in the art, at the time the invention was made, to further modify the method taught by the combined teachings of Shah and Chen et al. by removing the solvent using the two-step procedure of Tice et al., with a reasonable expectation of success. The motivation to do so is provided by Tice et al., who teach that the two-step procedure results in higher levels of active agent as compared with the conventional one-step procedure.

Applicants contest the assertion that the skilled person having read Shah and Tice would have had any reason to modify the single-step method of Shah to include the multi-step method of Tice.

Shah places a clear emphasis on the importance of using only a single step (direct lyophilization) on the final emulsion or suspension. The Background section of Shah refers expressly to the same Tice patent (i.e., U.S. Pat. No. 4,389,330) that is cited as a secondary reference in the present obviousness rejection. In its reference to Tice, Shah states that the solvent evaporation technique (as described in Tice) “is often not preferred because active

ingredient is often lost during the solvent extraction process” (Shah at col. 2, lines 11-12). In summarizing the importance of direct lyophilization to his methods, Shah states that his one-step method “provides several significant advantages over the processes described in the art” (Tice having been explicitly referenced as a prior art method) that include ease of manufacture of the active ingredient loaded microparticles, provision of sustained release formulations that maintain the activity and integrity of the active ingredient during release, and attainment of higher yields, high loading, and higher loading efficiencies (Shah at column 2, line 56, to column 3, line 5). In addition, Shah states that “the present process is more refined and simpler than those described in the art, and the activity and integrity of the active ingredient is maintained throughout the process” (Shah at column 3, lines 13-16).

Shah's comments on the advantages of its single-step direct lyophilization method as compared to the multi-step solvent evaporation process of Tice directly contradict the remarks in the Office Action (at page 9) asserting that “[s]uch teachings, would motivate one of skill in the art to sacrifice simplicity for quality, i.e., to modify Shah's method by using the Tice's two-step solvent removal method.” Shah clearly states that its method results in higher yields, high loading, and higher loading efficiencies. As a result, Shah teaches that its method is superior to those in the art (such as Tice) because of both (i) simplicity of manufacture, and (ii) the quality of the resulting microparticle product. Contrary to the suggestion in the Office Action, the skilled person having read the cited references would have concluded that Shah teaches methods of preparing microparticles having all-around superior characteristics (as compared to those of Tice).

In view of the teachings of Shah and Shah's direct commentary on Tice, the skilled person would have been strongly discouraged from modifying Shah's method by adding Tice's two-step solvent removal method. Shah teaches that such a modification would have been expected to result in both a more cumbersome method as well as the production of a lower quality product. As a result, the teachings of Shah would have failed to provide the requisite reason for making the modification proposed in the Office Action.

The remarks above establish that the skilled person having read Shah and Tice would have had no reason to make the modification proposed in the Office Action. In addition to the failure of the references to establish a *prima facie* case of obviousness, the comments of Shah

regarding the drawbacks of Tice actually teach away from making the Examiner's proposed modification. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994). In this case, the skilled person would have been expressly discouraged (by the teachings of Shah) from modifying Shah's method to include Tice's two-step solvent removal method.

The Office Action asserts (at pages 8-9) that the alleged teaching away portion of Shah "only teaches that Tice's method is not preferred for water-soluble drugs" and that "the instant case pertains to nucleic acids and not to water-soluble drugs." Applicants note that nucleic acids are water soluble and this property is well known to those of skill in the art. This fact only underscores the teaching away of Shah with respect to use of Tice's two-step solvent removal method in the preparation of nucleic acid-containing microparticles.

In view of the forgoing remarks, applicants respectfully submit that the skilled person would have had no reason to make the modifications to Shah suggested in the Office Action. As a result, the combination of Shah, Chen, and Tice do not render obvious the claimed methods. Applicants request that the Examiner withdraw the rejection of independent claim 1 and claims 2-4, 12-17, 19-25, 32-46, 48-50, 54, and 55 that depend therefrom.

At pages 9-10 of the final Office Action, claims 1-6, 12-17, 19-25, 32-46, 48-50, 54, and 55 were rejected as unpatentable over Shah taken with Chen and Tice in further view of Parikh et al., U.S. Patent No. 5,660,858 ("Parikh").

The Office Action cited Parikh as describing the use of lipid stabilizers (recited in dependent claims 5 and 6) and asserted that "[i]t would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Shah taken with Chen et al. and Tice et al. by including lipid stabilizers".

As detailed above, the combination of Shah, Chen, and Tice does not render obvious the method of independent claim 1. Parikh provides nothing that supplements the deficiencies of Shah, Chen, and Tice or renders obvious the method of independent claim 1. Accordingly, once

independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

At pages 10-12 of the final Office Action, claims 1-4 and 7-55 were rejected as unpatentable over Shah taken with Chen and Tice in further view of Hartounian et al., US20020039596 ("Hartounian") and Hedley et al., U.S. Patent No. 5,783,567 ("Hedley").

The Office Action cited Hartounian and Hedley as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Shah, Chen, and Tice in view of Hartounian and Hedley to arrive at the methods of these dependent claims.

As detailed above, the combination of Shah, Chen, and Tice does not render obvious the method of independent claim 1. Hartounian and Hedley provide nothing that supplements the deficiencies of Shah, Chen, and Tice or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

CONCLUSIONS

Applicants submit that all claims are in condition for allowance, which action is requested. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 08191-0012002.

Respectfully submitted,

Date: June 18, 2009

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